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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,093	06/15/2006	Andreas Nandy	MERCK-3179	1555

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
06/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,093	NANDY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-12,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 3/02/09, is acknowledged.

2. Claims 1-19 are pending.

3. Claims 1-9 and 14-17 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 10-12 and 18-19 are under consideration in the instant application as they read on the Lol p 4 polypeptide encoded by SEQ ID NO:I or SEQ ID NO :3 and composition and medicaments thereof.

5. Applicant's IDS, filed 3/02/09, is acknowledged.

6. The Focke et al reference cited on the PTO-892, is provided as evidence in Applicant's Remarks. Accordingly, the reference will not be supplied.

7. The following new ground of rejections are necessitated by the amendment submitted 3/2/09.

8. 35 U.S.C. §101 states:

> *Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.*

9. Claim 10 is rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claim 10, as written, do not sufficiently distinguish over proteins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Purified" as disclosed on page 10, line 11of specification. See MPEP 2105.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

11. Claims 11-12 and newly added claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a composition comprising a polypeptide encoded SEQ ID NO 1 or SEQ ID NO: 3, does not reasonably provide enablement for: a polypeptide according to Claim 10 **as medicament** in claim 11; and **a pharmaceutical composition** of claim 12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 9/30/08.

Applicant's arguments, filed 3/2/09, have been fully considered, but have not been found convincing.

Applicant submits that their specification coupled with a skilled worker's knowledge, provides more than adequate guidance on how to make the claimed polypeptide molecules and use pharmaceutical compositions and medicaments comprising such polypeptides for immunotherapy. The specification provides both general and specific guidance regarding the specific epitopes in allergens and how such could be manipulated for reliable hyposensitisation. See, for example, the disclosure contained in the paragraphs bridging pages 6 and 7 of the instant specification and the reference article by Schramm et al., 1999, J. Immunol. 162:2406-2414. With respect to DNA vaccines, the specification explicitly teaches that "experimental evidence of allergen-specific influencing of the immune response has been furnished in rodents by injection of allergen-encoding DNA (Hsu et al., 1996, Nature Medicine 2 (5): 540-544)." Furthermore, the specification of the present application discloses specific immunotherapy or desensitization as therapeutic field for especially recombinant allergen proteins with higher purity and therefore reduced side effects than allergen proteins isolated from natural sources which are always mixtures of compounds. To this end, the specification discloses strategies to minimize the risks of side effects with the development of T-cell reactive fragments with reduced or no IgE-reactivity leading to hypoallergenic peptides (see, page 8, lines 15-26). The screening for T-cell and IgE epitopes were common knowledge at the priority date of the present application. Thus, a person skilled in the art would have been able to identify T-cell and IgE epitopes and produce hypoallergenic peptides. Nevertheless, also the classic approaches of specific immunotherapy and desensitization were applicable as a skilled person would have known the pharmaceutical effects and also the side effects and risks of an allergen protein administered to a patient and would have followed clinical recommendation protocols for specific immunotherapy and desensitization.

However, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to screen to identify the invention. Until the time when hypoallergenic peptides are found, then one skill in the art can make them. The claims fail to meet the enablement requirement for the "how to make and use" prongs of the U.S.C 112, 1st paragraph.

Applicant points to the specification on page 6, last ¶ and Focke et al FASEB Journal, 15:2042-44, 2001) for support the claimed medicament and pharmaceutical composition. Applicant points to the "immunization" section and the immunoglobulin reactivity data provided in Figs. 5 and 6 and Tables 3-5 of the article, to support the contention that the instantly claimed grass pollen allegens could be routinely manipulated and utilized as pharmaceutical preparations in a manner recited in the claims.

However, the MPEP also states that physiological activity can be considered inherently unpredictable. Further, in Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), the court states "If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis." In the instant case no efficacy has been show using the claimed polypeptide encoded by SEQ ID NO: 1 or 3 and the state of the art is that allergen immunotherapy is unpredictable due to the retention of B-cell epitopes within the allergen which confers a risk of IgE-mediated potentially life-threatening systemic reactions (Tarzi et al of record).

Applicant submits that the specification provides an enabling disclosure on the claimed allergenic properties of the recombinant, grass pollen allergen polypeptides of the instant invention. Therefore, the specification's express teaching that the claimed compounds are pharmaceutically useful is clearly credible as required. The PTO's contentions regarding non-enablement are especially weak in view of the detailed disclosure contained in Applicants' own specification and the state of the art before the earliest filing date of the instant application. Withdrawal of the rejection is respectfully requested.

However, at issue is whether or not the claimed composition would function as pharmaceutical composition or medicament. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success. The lack of any working examples is exacerbated because the invention is in a highly unpredictable art-allergen immunotherapy- and while the level of skill of in the art may be high,

the state of the prior art is that it is in fact unknown and untested what are the underlying physiologic bases of the therapeutic effects of Lol p 4 polypeptide in the diagnosis, prevention or remediation of allergies in the triggered by group 4 allergens.

Applicant criticize the Tarzi (Expert Opinion in Biol, Then, 2003) reference use by the Examiner to support the non-enablement of the claimed therapeutic efficacy of the claimed Lol P 4 polypeptide. Applicant submits that even Tarzi discloses the therapy of allergic diseases with specific immunotherapy or desensitization in general being effective and successfully applied for many years. See, the last paragraph at page 617 of the cited reference. Moreover, in Gefter et al. (USP 6,795,234), which was cited by the PTO in reference to an art reiection, the complete third and fourth paragraphs in the "BACKGROUND OF THE INETNION" (especially, col. 1, lines 26-45) discloses that the risk of systemic reactions like anaphylactic shock can be effectively minimized in individuals via specific immnnotherapy, wherein pharmaceutical compositions comprising allergen polypeptides and/or vaccines comprising DNA sequences which encode such polypeptide allergens are utilized. As such, the PTO's contentions of non-enablement, based on the disclosure contained in Tarzi and/or Gefter is without merit.

However, Tarzi et al teach that to support the contention of non-enablement, the Office Action cites Tarzi (Expert Opinion in Biol, Then, 2003) to allege that "whole allergen immunotherapy is unpredictable." However, even Tarzi discloses the therapy of allergic diseases with specific immunotherapy or desensitization in general being effective and successfully applied for many years. See, the last paragraph at page 617 of the cited reference. Moreover, in Gefter et al. (USP 6,759,234), which was cited by the PTO in reference to an art reiection, the complete third and fourth paragraphs in the "BACKGROUND OF THE INETNION" (especially, col. 1, lines 26-45) discloses that the risk of systemic reactions like anaphylactic shock can be effectively minimized in individuals via specific immnnotherapy, wherein pharmaceutical compositions comprising allergen polypeptides and/or vaccines comprising DNA sequences which encode such polypeptide allergens are utilized. As such, the PTO's contentions of non-enablement, based on the disclosure contained in Tarzi and/or Gefter is without merit.

However, Tarzi et al teach that the retention of B cell epitopes in whole allergen preparations confers a risk of IgE-mediated systemic reaction, which complicate the treatment course of ~10% of individuals and may be life-threatening (see page 617, 2nd ¶). Further the `234 patent teaches that the that the densensitization therapy must be undertaken with extreme caution as the side effects may be significant or even fatal. The `234 patent concluded that this treatment is very time intensive, inconvenient and not without side effects or danger for the patient (see 1st col., lines 35-45).

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> *A person shall be entitled to a patent unless –*
> *(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

13. Claims 10-12 and newly added claims 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,759,234 (PTO-892; Reference A) for the same reasons set forth in the previous Office Action mailed 9/30/08.

14. Claims 10-12 newly added claims 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Bose et al. (PTO-892; Reference W) for the same reasons set forth in the previous Office Action mailed 9/30/08.

15. Claims 10-12 newly added claims 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Zhou et al. (PTO-892; Reference V) for the same reasons set forth in the previous Office Action mailed 9/30/08.

16. Claims 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. WO 96/07428 (PTO-892; Reference N) for the same reasons set forth in the previous Office Action mailed 9/30/08.

Applicant's arguments, filed 3/2/09, have been fully considered, but have not been found convincing.

Applicant submits that the cited Gefter patent applications, Bose et al., Zhou et al, and the WO 96/07428 merely disclose in a Lol p 4 isolated from natural sources. Allergen protein isolated form natural sources are always mixtures of several compounds and allergens and isoforms thereof and never a pure form of the protein. This is the advantage of recombinanlly prepared proteins and the inventors of the present invention were the first to clone and to determine the DNA sequence of Lol p 4. Thus, the DNA sequences in accordance with SEQ ID NO: 1 and 3 are not inherent in the reference Lol p 4 as the references do not disclose DNA molecules at all and also do not disclose amino acid sequences of a specific isoform of Lol p 4. The references are also silent with respect to recombinant polypeptides. See, the subject matter of the new claims. As such, the PTO's contentions are without merit.

However, while newly added claim 18 is constructed as product by process. However, the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985), MPEP 2113. It is Applicant burden to show that the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.

However, besides applicant assertion that the prior art do not disclose amino acid sequences of a specific isoform of Lol p4, Applicant fails to provide any showings that the referenced protein is not the claimed Lol p4 encoded by SEQ ID NOs: 1 or 3. Since the office does not have a laboratory to test the reference Lol p IV protein, it is applicant's burden to show that the reference Lol p IV protein is not encoded by SEQ ID NO:1 or SEQ ID NO:3 as recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). The disclosure

of a polypeptide encoded by SEQ ID NO: 1 or 3 is only further characterization of otherwise old product. The mere sequencing of a product, by itself, does not render the product novel.

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 29, 2009

/Maher M. Haddad/
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